[REVIEW]

Quality of Life in Patients Suffering from Insomnia

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ABSTRACT

Objective: Systematic review of the literature pertaining to quality of life studies in adults suffering from insomnia, by specifically addressing the following questions: 1) What is the impact of insomnia on quality of life? 2) To what extent do comorbid conditions affect quality of life in patients with insomnia? 3) What is the impact of insomnia treatment on quality of life?

Design: Our search was conducted using the MEDLINE/PubMed and PsycINFO databases from the past 25 years (1987–2012), using the keywords "Insomnia" AND "Quality of Life," "QOL," "Health-related quality of life," or "HRQOL." Fifty-eight studies were selected for inclusion by two physicians who reached a consensus about the studies to include in this review.

Results: The literature reveals that quality of life is severely impaired in individuals with insomnia, comorbid conditions significantly affects quality of life negatively, and sleep restoration techniques, including cognitive behavioral therapy and medications, are successful at improving quality of life. However, restoration of quality of life to community levels is still unclear.

Conclusion: Insomnia and its comorbidities negatively affect an individual's quality of life, and different modalities of treatment can produce improvements in physical and psychological wellbeing and quality of life. More research is needed to develop more interventions that specifically focus on improving quality of life in patients suffering from insomnia.

INTRODUCTION

The World Health Organization (WHO) defines quality of life (QOL), as individuals' perception of their position in life, in the context of culture and value systems in which they live, and in relation to their goals, expectations, standards, and concerns.[1] This conceptual framework is translated into patient-reported ratings of the degree of satisfaction one has with health, social, occupational status, and other life involvements. Hence, high QOL ratings are reflective not only of symptom reduction but also an overall improvement in the self-evaluation of one's own health. This is especially important in assessing whether interventions have accomplished the goal of health restoration and not merely symptomatic treatment. Quality of

life may be a more reflective lens through which to view the consequences of insomnia; it allows one to understand the significant impact this disorder can have on the daily lives of the people it affects,[2–5] as impairments in QOL typically are cited as the impetus for seeking treatment.[6]

Insomnia is defined as difficulty with sleep initiation or sleep maintenance, early morning awakenings or nonrestorative sleep, according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision* (*DSM-IV-TR*) criteria. Such symptoms hold the potential to drastically affect the patient's ability to maintain a sense of wellbeing and perception of self-satisfaction with health, occupational, and social functioning. Consequently, insomnia is commonly linked to a diminished QOL status for both primary (syndromic) and secondary (symptomatic) insomnia.[5] Insomnia is highly prevalent in the general population. Research reveals a prevalence of approximately 30 percent of insomnia symptoms with a range of 10 to 40 percent, depending on how insomnia is defined.[7] Somewhere between 10 and 18 percent of these individuals consider their difficulties with sleep to be severe and chronic.[8] Overall, insomnia is more common in women than in men, and its prevalence increases with age in both sexes.[5] Insomnia may be a primary disorder (a syndrome) or secondary to a variety of physical or psychiatric illnesses (e.g., sleep apnea, depression, anxiety), environmental factors (e.g., noise levels, temperature, seasonal changes) and/or psychosocial issues (e.g., current or upcoming stressors). Identifying and treating potential underlying conditions are priorities in the management of insomnia. Insomnia is associated with a number of adverse medical, social, and psychological consequences leading to QOL impairments.

The World Health Consensus report on sleep found relatively little research specifically devoted to the subject of evaluating QOL in insomnia.[9] The goal of this review is to examine QOL in patients with insomnia through an in-depth review of the topic's published literature. While recent reviews have focused on how insomnia affects some aspects of QOL, such as daytime functioning, sleep quality, neurocognitive functioning, and societal burden,[2] QOL generally,[3] and QOL within the context of economic and public health consequences,[4] information about the extent of the role of comorbidities as well as the impact of treatment of insomnia on QOL remain largely unaddressed. Additionally there is lack of investigation of studies that compare different treatment modalities and the differential impact on QOL.

This paper aims to answer the following three questions: 1) What is the impact of insomnia on QOL? 2) To what extent do comorbid conditions affect QOL in patients with insomnia? and 3) What is the impact of insomnia treatment on QOL?

This review will attempt to answer the above questions via a systematic review of the published literature pertaining to QOL in insomnia. It will also identify knowledge gaps in the field and propose future areas of research that may deepen our understanding of this topic.

METHODS

Data sources. A systematic literature search was conducted using the MEDLINE/PubMed and PsycINFO databases for the past 25 years (1987–2012). We used the keywords "insomnia" AND "quality of life," "QOL," "health-related quality of life," or "HRQOL." The reference list of identified papers and prior reviews were manually reviewed for additional studies. The initial search yielded 427 articles. The search was then narrowed to studies that only included measurement of quality of life. This narrowed search yielded 150 articles.

Study selection criteria. Two physicians reviewed the 150 abstracts using the following inclusion criteria: 1) articles in English or with an available published English translation, 2) publication in a peer-reviewed journal, 3) studies of humans, 4) studies (of any design) that focused on insomnia (not other sleep symptoms), and 5) studies that used at least one QOL measure or domains derived from QOL measures. Both physicians then conducted, independently, a focused review using the full text articles of studies that met the above criteria. The reviewers then reached a consensus about the studies to include in this manuscript.

Data extraction and yield. The study selection process yielded 58 articles meeting the aforementioned selection criteria. Research methodology and key findings were derived from the full text and the tables of the selected studies. The literature search and selection methodology are depicted in Figure 1.

QOL measures in insomnia. *General QOL measures used in insomnia.* The Medical Outcomes Study Short Form-36 (SF-36) is a very widely used scale in evaluating health-related QOL (HRQOL) in a variety of medical/psychiatric conditions and in insomnia.[10–14] The SF-36 is a 36-item generic QOL measure that assesses eight domains specific to HRQOL: 1) physical functioning, 2) role limitation due to physical health problems (role physical), 3) body pain, 4) general health perceptions, 5) vitality, 6) social functioning, 7) role limitations due to emotional health problems (role emotional), and 8) mental health.[15,16] All health measures are scored on scales of 0 to 100, with higher scores indicating better health. Community norms are set at a mean score of 50 (SD=10) on each of its two components: physical component score (PCS) and mental component score (MCS). The SF-36 has two abbreviated versions: the 12-item SF-12 and the eight-item SF-8. There are several advantages to using the SF-36, such as the following:

Reliability and validity have been extensively tested in many different populations; norms have been generated for disease-specific and general population; it is easy to complete; it allows for comparisons across disease states; and it has been shown to be sensitive to insomnia-related changes.[17–19] Limitations associated with the SF-36 include decreased sensitivity at extremes (either good or bad) and its lack of specificity to the illness it measures.[19]

The Quality of Life Enjoyment and Satisfaction Questionnaire Short-Form (Q-LES-Q)is a 16-item scale with a total score ranging from 0 (lowest QOL) to 100 (highest QOL) with established community norms mean score of 78.3 (SD=11.3).[20,21] The Q-LES-Q has been used in a wide variety of research studies of psychiatric disorders including insomnia.[22]

The World Health Organization Quality of Life—Brief Form (WHOQOL-BREF) is a 24-item questionnaire covering four domains (physical health, psychological health, social relationships, and environment)[23] has been used more commonly to measure QOL in other disorders where insomnia is also present.

The EuroQol-5 (EQ-5D) is a five-item QOL questionnaire covering five domains (mobility, self-care, usual activity, pain and anxiety/ depression) and has been used in comorbidity studies.[24] Other investigators also used the QOL inventory, a 31-item questionnaire specifically designed for the study which includes questions related to sleep, cognitive function, daytime performance, social and family relationships, and health.[4] Details of the psychometric properties of the general QOL measures appear in a previous article by the authors.[25]

Insomnia-specific QOL Measures. Léger et al[19] developed a measurement tool, the Hotel-Dieu-16 (HD-16), to specifically evaluate QOL in those with varying severity of insomnia. Unlike the aforementioned instruments, the HD-16 was designed to control for comorbid illness that may confound the association between QOL and insomnia and was constructed based on interviews with 20 patients with 'severe' insomnia (two or more complaints of insomnia in the past month) and validated by applying the scale to patients classified as "good sleepers" (n=391), "mild insomniacs" (n=422), and "severe insomniacs" (n=240). Five dimensions (physical energy/the will to carry out tasks, cognition, social, and psychological) of QOL are evaluated over 43 questions. While this study has some limitations, including nonspecificity of several items (i.e., evaluates symptomatology common to many other disease states) and only one evaluated sample, thus the generalizability remains unproven; the face validity of the study appears sound. The authors concluded that an insomnia-specific QOL measurement is better able to capture the deficits in functioning and QOL directly attributable to insomnia and may better evaluate treatment outcome.

The Quality of Life of Insomniacs questionnaire was developed by Rombaut et al[26] to specifically evaluate QOL in insomnia. This instrument has been used in a few studies, and it has not been expanded into clinical or research settings.

Other QOL measures used in insomnia. The Nottingham Health Profile (NHP, 38-item covering 6 domains)[27] and the Sickness Impact Profile (SIP, 136 items covering 12 domains), both of which are generic measures, have also been used to detect QOL changes associated with insomnia.[18,19] McCall et al[22,28] used the daily living and role functioning (DLRF) and relationship to self and others (RSO) subscales of the Behavior and Symptom Identification Scale (BASIS-32) to assess QOL. The DLRF and RSO subscales have been shown to differentiate depressed patients with insomnia from those without insomnia.[22]

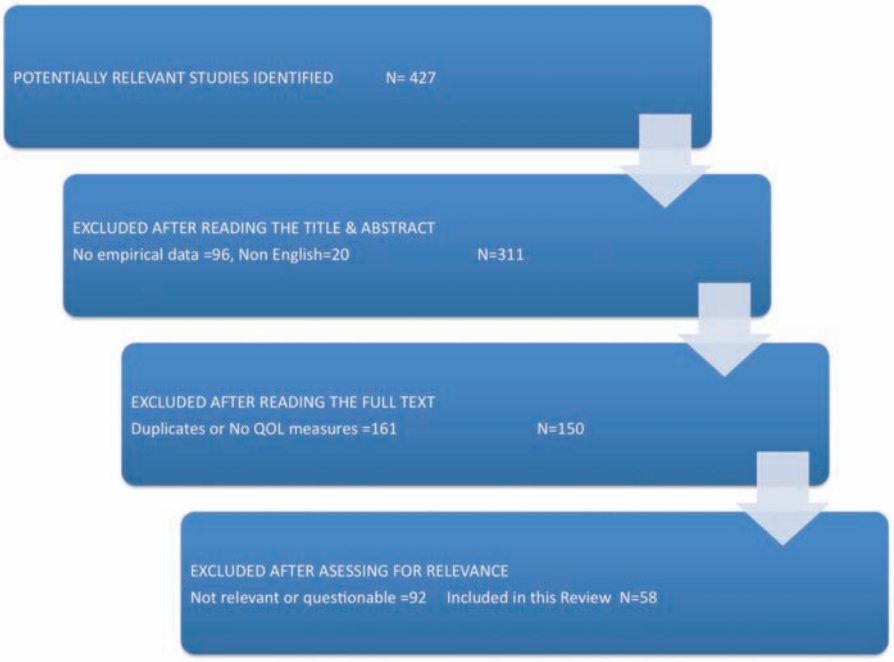

FIGURE 1. Quality of life in insomnia literature search results

RESULTS WHAT IS THE IMPACT OF INSOMNIA ON QOL?

Insomnia has a large impact on an individual's ability to maintain work, physical, and social performance as well as overall quality of life, as shown by the findings from reviewed studies (Table 1).

Studies using the SF-36 to assess insomnia and its impact on QOL showed that individuals with insomnia reported poor QOL.[10–13,16] Zamitt et al[11] used several instruments to evaluate the impact

of insomnia on QOL in a sample of 261 "insomniacs" compared to a control group of 101 good sleepers. Individuals with irregular sleep patterns, sleep apnea, restless leg syndrome, periodic limb movement disorders, a history of psychiatric illness, alcohol and substance abuse, epilepsy, and human immunodificiency virus infection were excluded from the study. To evaluate QOL, Zamitt et al[11] used the SF-36 and the QOL inventory. The results showed a significant difference between the two groups (p<0.0001 MANOVA) on all eight SF-36 subclasses. In comparison to "good sleepers," individuals with insomnia reported more health concerns that limited physical activity, caused more body pain, and caused more emotional difficulties.

Léger[17] explored the effect of insomnia on daytime functioning using the SF-36 to evaluate the QOL of three matched groups of 240 subjects with severe insomnia, 422 with mild insomnia, and 391 good sleepers. It was found that those with severe insomnia had lower QOL scores in the above eight dimensions of SF-36 than did those with mild insomnia and good sleep patterns. Mental status and emotional state were worse in both the severe and mild insomnia groups compared to the good sleepers.[17] In a study of insomnia and quality of life, Katz and McHorney[29] examined 3,445 patients diagnosed with chronic medical and psychiatric conditions. The results showed that patients with insomnia have lower quality of life, measured by the SF-36, independent of the presence/absence of a comorbid chronic illness. Furthermore, the study found that the effect of insomnia on quality of life is equal in severity to the effect of any chronic illness, such as congestive heart failure or clinical depression. Similarly, decreased QOL as a function of insomnia was shown to be comparable to QOL impairment due to chronic medical conditions, using the Nottingham Health Profile (NHP)[27] and the Sickness Impact Profile (SIP).[18,19]

In summary, insomnia negatively affects individuals' quality of life and could cause increasing impairment in QOL with increasing severity of sleep disturbance.[3,30–35]

WHAT IS THE IMPACT OF COMORBIDITIES ON QOL IN INSOMNIA?

Insomnia commonly exists in the presence of medical, psychiatric, and psychosocial stressors.[36] Vallieres et al[37] found that unemployment, recent death of a friend/family member, recent end of a relationship, and personal illness are the most common precipitants for short-term insomnia (less than one month). Underlying stress may be one of the factors contributing to insomnia and could contribute independently to impairing an individual's quality of life.[29] Stressors may also exacerbate the severity of insomnia as well as other comorbid conditions, which in turn may have several downstream effects on QOL and ability to function. Moreover, studies show that individuals suffering from insomnia have a greater chance of developing depression and anxiety leading to further QOL deterioration.[62] Research shows that insomnia was often comorbid with chronic illnesses or depression.[31]

Psychiatric comorbidities. It is estimated that insomnia affects anywhere from 50 to 80 percent of the treatment-seeking psychiatric population,[38] highlighting the importance of psychiatric comorbidities and/or causes of psychopathology. Additionally, 30 to 50 percent of the aforementioned population that suffers from chronic insomnia has one or more of the following psychiatric disorders: major depressive disorder, mania/hypomania, an anxiety disorder (phobias, obsessive-compulsive disorder, panic disorder, generalized anxiety disorder) and/or a substance abuse/dependence disorder.[39]

Depression. Sleep disturbance is an important component in the clinical presentation of depressive disorders. Insomnia is a particularly frequent complaint as it is reported by nearly 85 percent of depressed patients.[40] Unfortunately, insomnia remains the most commonly unresolved symptom of depression even after mood improvement following selective serotonin reuptake inhibitors (SSRIs) treatment.[22] Many depressed patients attribute low daytime functioning, including poor concentration and memory, decreased reaction time and coordination, fatigue, mood disturbance, and anxiety to inability to obtain an adequate amount of nighttime sleep or sub-par quality of sleep.

A study performed by McCall et al[22] was designed to measure the impact of insomnia on the quality of life of inpatients with depression. The results showed lower QOL ratings in patients with comorbid insomnia. This difference was especially prominent in those using a measure of self-report, the Beck Depression Inventory (BDI), as compared to the clinician-rated Hamilton Rating Scale for Depression (HRSD). In a study of residual symptoms in depression, approximately 40 percent of patients receiving fluoxetine reported symptoms compatible with nonrestorative sleep.[41] Compared to sleep disturbances related to initiation or maintenance of sleep, nonrestorative sleep is associated with greater daytime functional impairment. Therefore, targeting insomnia in depression may increase daytime performance and overall QOL.

Anxiety disorders. Generalized anxiety disorder (GAD) and insomnia commonly coexist, with at least 66 percent of patients with GAD experiencing comorbid sleep disturbances.[42] Similarly, GAD is the most common psychiatric disorder among patients with insomnia.[42] Brenes et al[43] found that 90 percent of older adults with GAD reported moderate to severe insomnia.[43] Individuals with significant insomnia often also experience somatic manifestations of psychiatric illness, such as elevated physiological

TABLE 1. Impact of insomnia on QOL

REFERENCE	MEASURE	N	SUMMARY OF FINDINGS
Zammit et al (1999)[11]	SF-36	261 insomnia subjects, 101 controls	Insomnia patients had significantly lower SF-36 scores compared to controls (p< 0.0001).
Schubert et al (2002)[12]	SF-36	2,800	In a population of older adults, 26% reported 1 insomnia symptom, 13% reported 2, and 10% reported 3. SF-36 decreased on all 8 domains as the number of reported symptoms increased (p< 0.0001).
Stein et al (2008)[13]	SF-36	1,359	Chronic physical illness was associated with poorer HRQOL (p<0.0001). Psychotropic medications use was associated with lower scores on SF-36 MCS (p=0.0001) and SF-36 PCS (p=0.015) in women (controlling for age and number of comorbid illnesses).
Léger et al (2001)[17]	SF-36	240 insomnia subjects and 391 good sleepers	This study compared good sleepers (GS) to patients with severe insomnia (SI)—Physician visit with insomnia complaint: 0% GS v. 18% SI (p<0.0001); regularly taking sleeping pills: 0% GS v. 28% SI (p<0.0001); hospitalizations (past 12 mo.): 9% GS v. 18% SI (p=0.0017); on at least 1 medication: 44% GS v. 67% SI (OR=2.59); "Work error that could have serious consequences:" 6% GS v. 15% SI (p<0.001).
Katz and McHorney (2002)[29]	SF-36	3,445	34% had mild insomnia and 16% had severe insomnia at baseline. 59% (95% CI, 55%-63%) of patients' with mild insomnia and 83% (95% CI, 78–88%) with severe insomnia at baseline still had problems at 2-year follow-up. Mild and severe insomnia were associated with decreases in physical health perception (mild: OR=2.0; severe: OR=5.1), vitality (mild: OR=2.4; severe: OR=7.4), and mental health (mild: OR=3.5; severe: OR=10.2) domains.
Stein et al (2002)[31]	SF-36	4,181	Sleep problems were found to be associated with physical (AOR=1.21, 95% CI=1.01–1.45) and mental health problems (AOR=3.58, 95% CI=2.95–4.35) especially in those with comorbid physical health issues. The co-occurrence of insomnia was independently associated with poorer ratings on the SF-36 PCS (p< 0.001) and increased the odds of 1 or more days taken off from work in the past 30 days due to physical problems (AOR=1.55, 95% CI=1.20–1.98) by 50%.
Hatoum et al (1998)[32]	SF-36	1,100	Insomnia with reported impairments in daytime functioning was associated with significant QOL deficits across all domains (p<0.001). Compared to patients without insomnia, patients with problems with quality/quantity of sleep (no reported daytime symptoms) demonstrated significantly lower scores on the PCS (p<0.001) and the body pain (p=0.01) subscale.
Guereje et al (2009)[34]	WHOQOL-Bref	2,152 elderly Nigerians	Difficulty initiating or maintaining sleep and early AM awakening were associated with physical, psychological, social, and environmental subscales and overall QOL (p<0.05).
Lee et al (2009)[35]	SF-36	397	Sleep disturbance and daytime fatigue were associated with increased likelihood of low scores on the following subscales: physical functioning, AOR=6.10; physical health problems, AOR=8.28; bodily pain, AOR=6.41; general health, AOR=5.88; vitality, AOR=17.09; social functioning, AOR=5.46; and mental health, AOR=12.83.

QOL: quality of life; SF-36: Medical Outcomes Study Short Form-36; HRQOL: health-related quality of life; MCS: mental component score; PCS: physical component score; OR: odds ratio; CI: confidence interval; AOR: adjusted odds ratio; WHOQOL-Bref: World Health Organization Quality of Life—Brief Form

symptoms of arousal (e.g., dizziness, headache, weakness, fatigue, palpitations, and gastro-intestinal distress).[44] Moreover, patients with insomnia report more attention disorders and memory complaints.[45] This may lead to impaired concentration and increase the risk of traffic accidents as well as fatigue and daytime sleepiness—symptoms associated with poor QOL.

Veterans returning from combat have been shown to demonstrate high rates of posttraumatic stress disorder (PTSD) and traumatic brain injury (TBI),[46,47] both of which are associated with a high prevalence of insomnia.[48] Additionally, all three diagnostic subcategories of PTSD, re-experiencing, avoidance, and hyper-arousal, may factor into the development of PTSD as they are associated with poor sleep hygiene and/or may be the impetus for frequent awakenings or delayed sleep initiation. In a study by Wallace et al[49] comparing the differential effects of PTSD with or without comorbid mild TBI (mTBI) on sleep and daytime functioning, the authors compared characteristics of sleep between healthy sleepers (control), individuals with insomnia plus PTSD plus TBI combined and individuals with insomnia plus PTSD alone. Although those participants with PTSD plus mTBI demonstrated similarities in type of insomnia experienced, short duration of sleep, and severity as compared to PTSD alone participants, the PTSD plus mTBI group indicated greater daytime sleepiness although they spent more of the night sleeping.[49] This is an important finding as insomnia due to decreased duration of sleep has been associated with poor HRQOL outcomes, such as increased use of the healthcare system, increased morbidity and mortality due to physical illness, and reduced work productivity.[49]

Childhood-related psychiatric disorders. Psychiatric illness in childhood can also have lifelong consequences on sleep quality and quality of life. Poon and Knight[50] investigated the downstream impact of childhood abuse/neglect on subjective feelings of sleep difficulty and the secondary effect that this has on perceived quality of life in adulthood. The authors postulated that neglect and abuse in childhood promote a neural set-up for poor attachment with hindrance of the development of positive interpersonal relationships later in life. The anxiety that this engenders in combination with heightened stress reactivity can contribute to insomnia secondary to the stress of psychosocial issues. This could further impact QOL and the ability to cope with emotional strain as well as diminish the ability to foster and maintain social relationships. Parental emotional abuse is associated with adulthood sleep complaints, which is consistent with indices of insomnia associated with emotional and interpersonal stress.

Medical comorbidities. Individuals with insomnia have 60-percent greater healthcare costs as compared to the general population due to over-utilization of the healthcare system.[51] This is evidenced by greater number of visits to the emergency department and outpatient physicians, increased use of pharmacotherapy, and more laboratory tests ordered,[52] proving to be a great economic and healthcare burden.[53] Of patients seen in primary care settings, approximately 10 percent suffer from chronic insomnia.[54]

Cancer. Insomnia affects up to 50 percent of cancer patients, contributing to feelings of fatigue, and possibly immunosuppression.[55,56] In a cross-sectional study of 120 elderly patients with cancer, Cheng and Lee[55] found that those with a symptom cluster of insomnia, pain, and fatigue reported the lowest QOL, based on Functional Assessment of Cancer Therapy (FACT-G) scores and experienced the greatest decrements in functioning. They concluded that as 5.5 to 18.8 percent of elderly cancer patients have co-occurrence of the aforementioned symptom cluster, the combined impact of the three serve to decrease QOL and perceived and actual functioning. Further research needs to be done to study the individual impact of pain, fatigue and insomnia on QOL and functional status in this unique population.[55]

Neurological disorders. Insomnia may also exacerbate symptoms of TBI possibly due to injury to the neural circuitry that regulates sleep, side effects of medications used to treat complications of TBI, or comorbid psychiatric, pain, or medical disorders.[49] Insomnia may further contribute to worsening symptoms of TBI by impeding the healing process that occurs during sleep. The estimated prevalence of insomnia in those with TBI varies widely from 21 to 93 percent.[57,58]

Comorbid insomnia is also a common problem in those with neurodegenerative disorders, such as Parkinson's or Alzheimer's disease. In certain neurological conditions, insomnia may be considered a direct result of the disease itself or secondary to other factors associated with it, such as pain, depression, or treatment medications.[59] Caap-Ahlgren and Devlin[60] investigated the impact of insomnia on QOL in a population of 102 patients with comorbid Parkinson's disease and found that they had lower scores on each domain of QOL, as measured by SF-36, as compared to patients with Parkinson's disease with no insomnia.[60]

Patients admitted to the ICU. Insomnia is well recognized in the intensive care unit (ICU).[61] Despite exhibiting normal duration of sleep, patients usually demonstrate poor quality and abnormal patterns of sleep. Poor sleep quality can continue in patients after discharge.[62] There is evidence that even the recollection of the difficulties experienced while on an ICU can negatively impact sleep six months after discharge.[62] These sleep disturbances have been found to contribute to significant continuing decrements in HRQOL in all domains of the EuroQol-5 and to the inability to return to prior functioning.[62] Lack of treatment may contribute to impaired QOL.[63]

Congestive heart failure (CHF). In a study conducted by Krakow et al,[64] insomnia and sleep-disordered breathing (SDB) were the most common causes of sleep disturbances in patients with CHF. Additionally, Johansson et al[65] found that in elderly patients with CHF, 42 percent demonstrated SDB as compared to eight percent in those without CHF (p=0.001). In regard to insomnia, of those with comorbid CHF, 72 percent had difficulty maintaining sleep (as compared to 50% in non-CHF patients; p=0.05), and 25 percent exhibited daytime fatigue (as compared to 8% in non-CHF patients; p=0.05).65 The elderly patients that demonstrated symptoms of insomnia or SDB and comorbid CHF had worse QOL scores compared to those without CHF. Furthermore, decrements in the physical composite score of the SF-36 were associated with the following signs of insomnia (p<0.05): difficulty initiating or maintaining sleep, early morning awakening, and nonrestorative sleep. Nonrestorative sleep was also associated with a deficit in the mental health composite score (p<0.05).[65] A study to evaluate the impact of nasal dilator strips (NDS) on sleep quality, SDB, and QOL was done in nonobese adults with sleep disturbances. The participants consisted of 42 subjects in the treatment group and 38 subjects in the control group. At four weeks follow-up, the treatment group reported significant improvements in insomnia severity and sleep quality and improvement in Q-LES-Q (mean d=0.51), compared to small, statistically insignificant changes in the control group.[64]

Comorbid sleep disorders. Although sleep disorders such as obstructive sleep apnea (OSA), SDB, narcolepsy, snoring and restless leg syndrome/periodic limb movement are considered separate disease entities from insomnia, the co-occurrence of the two and their combined impact on QOL is important to consider. To study characteristics of insomnia and their impact on QOL in a population of patients with OSA and comorbid insomnia, Bjornsdottir et al[66] evaluated 824 patients with OSA and 762 healthy controls. In regard to symptoms of insomnia, they found that compared to their healthy counterparts, those with OSA encountered greater difficulties with sleep maintenance. They also found that women with OSA had greater sleep onset latency as compared to women without OSA. Additionally, increased difficulty initiating and/or maintaining sleep was associated with poorer QOL (SF-12). Individuals with OSA also demonstrated more impairment in physical and mental domains of perceived QOL.[66]

WHAT IS THE IMPACT OF TREATMENT OF INSOMNIA ON QOL?

As the impact of insomnia on health and wellbeing might be under-recognized, many patients do not seek medical care early in the course of sleep disturbance, resulting in a significant amount of under-treatment and inadequate treatment.[67] As 85 to 90 percent of chronic insomnia is attributable to comorbidities, including circadian rhythm disorders, physical and psychiatric illness, concurrent substance abuse, and/or pharmacotherapy for comorbid illness,[8] cessation of medication/drug use and/or treatment of the primary disorder may adequately address sleep disturbances that would lead to a downstream impact on QOL. Behavioral as well as pharmacological interventions play an important role in treatment and improvement of daily functioning and one's perception of QOL. The details of the reviewed treatment studies are shown in Table 2.

Pharmacological treatments. It has been shown that 5 to 8 percent of the general population use medications to aid in better quality, or greater duration of sleep.[8] There are three United States Food and Drug Administration (FDA)-approved drug classes for the treatment of insomnia: benzodiazepines, benzodiazepine receptor agonists, and melatonin receptor agonists.

Benzodiazepines. Benzodiazepines have been shown to be efficacious in reducing sleep onset latency and frequency/amount of nighttime awakenings. However, benzodiazepines have not been formally studied for their impact on QOL and their negative effects on next-day functioning (e.g., decreased memory and recall and daytime sleepiness), as well as the risk of tolerance and/or dependence when used long-term.[68]

Benzodiazepine receptor agonists (BRAs). BRAs, also known as nonbenzodiazepine sedative-hypnotics, have also shown efficacy in treatment of insomnia. They demonstrate the same hypnotic effects as benzodiazepines without the high propensity for dependence and development of tolerance.

There are also several randomized, controlled trials (RCTs) that have been conducted to evaluate the efficacy of these medications on insomnia and the effect they have on QOL. In a RCT of 458 patients (231 randomized to treatment, 227 randomized to placebo) studying the impact of a 14-day standing zoplicone regimen with an additional six weeks of medication per patient request, the patients randomized to zolpicone had similar improvement in the psychological wellbeing component and global QOL of the QOLI as compared to the placebo group. But the treatment group demonstrated significantly greater improvement in the activity, sleep, social, and work domains.[67] These improvements were maintained at two-month follow-up.

Walsh et al[69] evaluated the efficacy of eszopiclone on sleep disturbances (latency of sleep initiation, time to waking after sleep onset, and total sleep time) and QOL impairments. After six months of study medication consumption, the patients receiving eszopiclone demonstrated greater improvement in bodily pain, physical and social functioning, and vitality as measured by the SF-36, as compared

TABLE 2. Impact of treatment on QOL in insomnia

REFERENCE	MEASURE USED	N	INTERVENTION	DURATION	SUMMARY OF FINDINGS (*P* VALUES, ODDS RATIOS, PERCENTAGES, OR EFFECT SIZES)
Byles et al (2003)[16]	SF-36	209 chronic insomniacs	CBT vs. placebo	Follow up at 3, 6, 12 months	Patients receiving CBT had reductions in SF-36 domains: vitality at 3 mo. (p<0.01) and physical functioning (p<0.04) and mental health (p<0.02) at 6 mo. CBT group had reduced hypnotic use (p<0.001) and insomnia scores (p<0.01) at 12 mo. follow-up compared to placebo.
McCall et al (2010)[22]	BASIS-32 (subscales: DLRF, RSO, Q-LES-Q	60 depressed patients with insomnia	Open-label FLX, followed by FLX combined with either ESZ 3mg or placebo at bedtime	1 week open label FLX following by 8 weeks of FLX + ESZ or placebo.	The ESZ group demonstrated significantly greater improvement in QOL (DLRF:p=0.01; RSO:p<0.05; Q-LES-Q:p=0.08) as compared to the placebo group. Additionally, women demonstrated greater improvement in QOL at the end of treatment (DLRF:p<0.01; RSO:p<0.05; Q-LES-Q-:p<0.01) as compared to the men within the same treatment group. Both subscales of the BASIS-32 had moderate effect sizes (DLRF:0.62; RSO:0.44) and the Q-LES-Q had a small effect size (0.38).
Morin et al (2006)[68]	SF-36	10,430 Australian women	Pharmacotherapy	3 years	Difficulty sleeping at baseline was associated with the following SF-36 domains: general health perceptions (p=0.03), emotional role limitations (p=0.0007) and general mental health (p=0.0003) and use of pharmacotherapy for sleep at baseline was associated with: physical functioning (p=0.0005), bodily pain (p=0.02), vitality (p=0.01), social functioning (p=0.01) and general mental health (p=0.001).
Walsh et al (2007)[69]	SF-36, Work Limitations Questionnaire	830 with primary insomnia	ESZ (3mg) vs. placebo	6 months, 14 days post-treatment	ESZ group had significantly better scores on the SF-36 domains vitality & social functioning and physical functioning and the Work Limitations Questionnaire (across all domains) as compared to placebo (p<0.05). ESZ patients had higher SF-36 ratings on bodily pain, role physical, general health, and MCS at 6 mo. (p<0.05). The vitality domain showed the greatest improvement at 6 mo. (p<0.001).
Scharf et al (2005)[70]	Q-LES-Q	231 adults aged 65–85 years with primary insomnia	ESZ 1mg (n=72), ESZ 2mg (n=79), or placebo (n=80)	2 weeks	ESZ 2mg group had greater QOL (p<0.05), daytime alertness, and sense of well-being as compared to placebo on the following domains: physical health, mood, household activities, and leisure time activities.
Sasai et al (2010)[73]	SF-8	2,822 adults 20 years and older	None (survey)	N/A	Patients with insomnia had lower MCS than good sleepers (p<0.01). Use of sleep medications was correlated with PCS (OR=1.36). Insomnia was associated with higher risk of low MCS (OR=2.29) and PCS (OR=1.69). MCS and PCS scores significantly lower in patients with insomnia on sleep meds as compared to good sleepers (p<0.01).

SF-36: Medical Outcomes Study Short Form-36; CBT: cognitive behavioral therapy; BASIS-32: Behavior and Symptom Identification Scale; DLRF: daily living and role functioning; RSO: relation to self and others; Q-LES-Q: Quality of Life Enjoyment and Satisfaction Questionnaire Short-Form; FLX: fluoxetine; ESZ: eszopiclone; QOL: quality of life; MCS: mental component score; PCS: physical component score; OR: odds ratio

to those receiving placebo. They also demonstrated decreased sleep onset latency, increased time to waking, and total sleep time.[69] Scharf et al[70] corroborated these findings in an elderly population randomized to placebo or eszopiclone. In this subset of the population, the above sleep parameters as well as QOL showed improvement in the eszopiclone group on the following domains: household activities, leisure activities, mood, medication, and physical health, as measured by the Q-LES-Q.[70]

McCall et al[22] used the DLRF and RSO subscales of the BASIS-32 in addition to the Q-LES-Q to assess QOL in a population of individuals with comorbid unipolar depression and insomnia at baseline and following treatment with a combination of fluoxetine and eszopiclone or placebo. Following eight weeks of treatment with either fluoxetine plus eszopiclone or fluoxetine plus placebo, the eszopiclone group demonstrated significantly greater improvement in QOL as compared to the placebo group. Additionally, women demonstrated significantly greater improvement in QOL at the end of treatment compared to the men within the same treatment group. Both subscales of the BASIS-32 had moderate effect sizes (DLRF: 0.62; RSO: 0.44) and the Q-LES-Q had a small effect size (0.38).

Melatonin and melatonin receptor agonists. Melatonin is a hormone produced in humans by the pineal gland in the central part of the cerebrum. Melatonin agonists are safe, nonaddictive, sleep-inducing drugs that eliminate changes in the circadian rhythm. They can regulate sleep-wake cycles and re-adjust circadian rhythms.[71] In a review evaluating the safety of different pharmacotherapeutic

TABLE 2. Impact of treatment on QOL in insomnia, continued

REFERENCE	MEASURE USED	N	INTERVENTION	DURATION	SUMMARY OF FINDINGS (*P* VALUES, ODDS RATIOS, PERCENTAGES, OR EFFECT SIZES)
Dixon et al (2006)[74]	SF-36	209 adults with chronic insomnia using hypnotic drugs for at least 1 month	CBT "sleep clinic" group and a "no additional treatment" control group	3–6 month follow up	CBT patients had significant reductions in sleep latency, improvements in sleep efficiency, and reductions in the frequency of hypnotic drug use (all $P<0.01$) at 3- and 6-month follow-ups. CBT patients showed an improvement in HRQOL scores at 6 mo on the following SF-36 domains: physical functioning ($p=0.04$), emotional role limitation ($p=0.01$), mental health ($p=0.02$)
Van Houdenhove et al (2011)[77]	SF-36, CIS-20, GHQ, PANAS	138 with insomnia	CBT	Baseline, post-treatment, 6 months after treatment	High severity of sleep disturbance at baseline was associated with greater improvements in physical and mental HRQOL. Daytime functioning impairment: 74% pre-treatment, 40% post-treatment, 35% 6 mo follow-up. Physical HRQOL: moderate effect sizes from pre- to post-treatment (ES=0.582, $p<0.001$), and pre-treatment to follow-up (ES=0.739, $p<0.001$); Mental HRQOL: large effect sizes from pre- to post-treatment (ES=0.761, $p<0.001$), and pre-treatment to follow-up (ES=0.082, $p<0.001$)
Espie et al (2008)[79]	FACT-G (cancer-related QOL)	150 adults 18 years and older with chronic insomnia and comorbid breast, gynecological, prostate, or bowel cancer	CBT (five weekly 50 min sessions) vs. treatment as usual (control)	Baseline, 5 week treatment, 6 month follow-up	CBT was associated with improved QOL as compared to treatment as usual in the following domains: physical (post-treatment $p=0.004$, follow-up $p<0.001$), social (post-treatment, $p=0.036$), and functional (post-treatment $p<0.001$, follow-up $p<0.001$).
Leger et al (1995)[81]	Self-administered 23-item questionnaire developed by study sleep experts (5 aspects of QOL-Safety, Professional, Leisure, Domestic, Relational, and Sentimental)	167 with insomnia, 381 good sleepers	Insomnia patients taking zoplicone for 12 months or more vs. good sleeper with no hypnotic use in the past 12 months	Cross-sectional	No differences found in quality of life between subjects with insomnia and good sleepers.
Hajak et al (2002)[82]	SF-36	789 with insomnia, aged 18–60 years	Zolpidem 10mg po 5 nights/week and placebo 2 nights/week vs. Zolpidem 10mg po continuously	14 days	Both groups demonstrated improvement with treatment. The continuous group demonstrated a greater increase in mean MOS score as compared to the discontinuous group ($p=0.005$).
Verbeek et al (2006)[83]	SF-36 SIP	Individual treatment: 18 chronic primary insomnia. Group treatment: 40 primary or secondary insomnia.	Individual CBT v. group CBT. CBT included psychoeducation, sleep hygiene, stimulus control, sleep restriction, relaxation exercises, and cognitive restructuring.	6 consecutive weekly sessions and follow-up sessions 1, 3, and 6 months	Both groups demonstrated significant improvement in QOL on the SIP: pre- to post-treatment ($p=0.000$) and from pre-treatment to follow-up ($p=0.025$).

SF-36: Medical Outcomes Study Short Form-36; CBT: cognitive behavioral therapy; CIS-20: Checklist Individual Strength; GHQ: General Health Questionnaire; PANAS: Positive Affect Negative Affect Schedule; ES: effect size; BASIS-32: Behavior and Symptom Identification Scale; DLRF: daily living and role functioning; RSO: relation to self and others; Q-LES-Q: Quality of Life Enjoyment and Satisfaction Questionnaire Short-Form; FLX: fluoxetine; ESZ: eszopiclone; QOL: quality of life; MCS: mental component score; PCS: physical component score; OR: odds ratio; HRQOL: health-related quality of life; FACT-G: Functional Assessment of Cancer Therapy; MOS: Medical Outcomes Study sleep module; SIP: Sickness Impact Profile

modalities in the elderly,[72] the authors concluded that melatonin agonists are safer to use than the traditional sedative-hypnotics that work on GABA receptors. The authors also found that melatonin receptor agonists also help to improve mood and quality of sleep in this population.

Other pharmacological interventions used for insomnia. No information is available on the impact of sedating medications, such as antidepressants (e.g., trazodone, mirtazapine, or tricyclics), antipsychotics (e.g., quetiapine, olanzapine, or chlorpromazine), or mood stabilizers (e.g., valproic acid, lamotrigine, or carbamazepine) on QOL in insomnia.

Potential negative effects of pharmacological interventions. In contrast to the above findings, sleep medications might have negative effects on QOL. In a survey of 2,822 individuals, Sasai et al[73] investigated the impact of insomnia and use of

any sleep medication on the mental health (MCS) and physical health (PCS) composite scores of the SF-8. The authors divided their sample into good sleepers, good sleepers taking sleep medication(s), individuals with insomnia, and those with insomnia taking sleep medication(s). Insomnia was found to be associated with poorer MCS and PCS (scores <50; 50 is the population average). In regard to both MCS and PCS, insomnia individuals taking sleep medications scored lower than insomnia individuals not taking sleep aids. Additionally, good sleepers taking sleep medications demonstrated significantly lower scores on the PCS as compared to insomnia individuals not using sleep medications. As the authors found that the use of pharmacotherapy to aid sleep was significantly associated with decrements in perceived physical health QOL, they concluded that sleep medication is independently associated with poorer physical QOL due to medication side effects.[73] This is very important to keep in mind, especially in patients who are taking sleep medications on a long-term basis.

Non-pharmacological treatments. *Cognitive behavioral therapy (CBT).* Several studies discuss the clinical efficacy and cost effectiveness of providing CBT for insomnia to long-term hypnotic drug users in general practice.[74,75] These studies concluded that CBT could indeed improve the sleep quality of long-term hypnotic users with chronic sleep disorders.

Among these was an RCT with two treatment arms—a CBT-treated 'sleep clinic' group and a 'no additional treatment' control group—and post-treatment assessments at three and six months.[75] Two-hundred and nine patients aged 31 to 92 years with chronic sleep problems were enrolled. Among CBT-treated patients, SF-36 scores showed significant improvements in vitality at three months ($p<0.01$). Not only was there a notable reduction in symptomatology and health-related quality of life during active CBT, but also these reductions were maintained following the cessation of CBT.[76]

In a RCT of 209 patients with chronic insomnia using hypnotics randomized to either CBT or control (care as usual in a general medical practice), Dixon et al[74] found that over the course of six months, those receiving CBT demonstrated significant improvement on emotional role limitation, mental health, and physical functioning domains of the SF-36 as compared to controls.

Van Houdenhove et al[77] investigated the impact of CBT for insomnia (CBT-i) on symptoms of insomnia and HRQL on 138 patients with primary insomnia. The authors found that CBT-i was effective in improving sleep disturbances, including sleep onset latency, such that percentage of daily use of pharmacologic sleep aids decreased. Additionally, daytime functioning improved and HRQOL improved, especially in the emotional domain such that scores approached normative scores. CBT-i appeared to have the greatest effect on HRQOL and daytime functioning in those with greater pre-treatment impairment in psychological QOL and daytime functioning and those with severe insomnia.[77]

CBT has been also shown to effective in cancer patients with insomnia. In 1993, Espie et al[78] highlighted practical behavioral and cognitive techniques to manage insomnia. Based on the same techniques, the investigators evaluated the impact of treatment of insomnia on QOL in 150 patients diagnosed with cancer who were not undergoing concurrent radiation/chemotherapy for greater than one month of the study.[79] The authors found that the CBT group demonstrated significant improvements on various measures of sleep, including latency of sleep onset and waking after sleep onset, as well as on the physical and functional domains of the FACT-G QOL assessment tool as compared to the treatment as usual group.[79]

Behavioral therapy. In a study comparing a three-component behavioral intervention (comprising stimulus control, relaxation and sleep hygiene) to sham biofeedback (placebo), Soeffing et al[80] found no difference in SF-36 scores between groups at the end of treatment. A limitation of this study was the evaluation of outcome measure QOL relatively early after initiation of treatment, such that effects of therapy on QOL may not have yet been apparent.

Other nonpharmacological treatments. No information is available on the effects of light therapy, exercise, or nutrition on the QOL of patients suffering from insomnia.

Treatment limitations. It is important to note that a small number of cross-sectional and noncontrolled studies demonstrated equivocal results of the effect of treatment of insomnia on QOL in regard to both pharmacological and behavioral treatments. These results were found in regard to "insomniacs" versus "good sleepers" with treatment with zolpiclone,[81] insomnia individuals treated continuously with nightly zolpidem or discontinuous zolpidem treatment,[82] and individual versus group CBT in insomnia individuals.[83] As there were several limitations in the study design in the aforementioned trials, such as the use of QOL domains instead of a well-validated measure of QOL and lack of control groups,[82,83] the results of these trials should be generalized with caution.

Nonpharmacological approaches for insomnia management are effective and can be first-line therapy.[68] However, CBT and other similar behavioral interventions are not readily available and that may limit their use, thus necessitating pharmacologic therapy.

Multimodal treatments combining sleep hygiene and CBT with hypnotic medications are helpful in relieving insomnia and improving their QOL.[3] More studies are needed to test the full effects of combined treatments on QOL in insomnia.

DISCUSSION

Insomnia produces clinically significant impairments in social and occupational areas of functioning, as evidenced by reduction of work productivity, frequent absenteeism, decreased cognition and mood, and increased morbidity of psychological and physical illness, accompanied by a greater healthcare burden due to chronicity of illness and direct and indirect costs to society. Furthermore, insomnia may predict future episodes of psychiatric illness. An individual's perception of loss of or decrements in functioning may provide the motivation to seek treatment, thus addressing impairments in QOL may more accurately reflect efficacy of treatment than indices of disease or illness. As QOL is assessed by questionnaires investigating personal satisfaction with physical and psychological wellbeing, further investigation into insomnia-specific measures is warranted. Several studies have shown the sensitivity of the generic SF-36 in evaluating of patients with insomnia, with an inverse association between degree of sleep disturbance and QOL ratings. These relationships remain after controlling for comorbid psychiatric and physical illnesses. Thus a combination of specific and generic measurement tools may be indicated to best capture the relationship between insomnia and domains of QOL. Successfully treating insomnia may improve a patient's HRQOL; however, medication side effects may also negatively impact perceived QOL. Patients with insomnia and comorbidities, including mood and anxiety disorders, cardiovascular, renal, respiratory, neurological disorders, cancer, acquired immunodeficiency syndrome, and chronic pain have poorer QOL. As chronic insomnia is associated with increased healthcare burden, increased morbidity and mortality, and decreased day-to-day functioning, addressing insomnia in comorbid psychiatric and medical illness is important. Treating both conditions may improve the outcome for insomnia, comorbidities, and QOL overall. Interventions that specifically target QOL in insomnia are highly needed. Additionally, there remains a paucity of studies that specifically utilized QOL as primary outcome measure, thus further controlled trials needs to be done to address related gaps in knowledge.

CONCLUSION

Quality of life in insomnia is significantly impaired affecting overall subjective sense of physical or psychological well-being. The effect of insomnia on QOL may be related to psychiatric or physical comorbidities, medications, and/or various psychosocial issues or may be illustrative of a primary disease effect. Due to the lack of biomarkers to measure disease progression in psychiatric illnesses, symptom severity is generally used to measure the illness activity. However, symptom improvement is not the sole indicator of improvement, as restoration of QOL remains a key indicator of wellness. There is evidence to support the positive treatment effect on QOL in patients suffering from insomnia. These studies suggest that addressing both insomnia and co-morbidities has the potential of improving both conditions. However, more work is needed to enhance our understanding of QOL impairment in insomnia and to develop more effective and specific ways to ameliorate it.

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